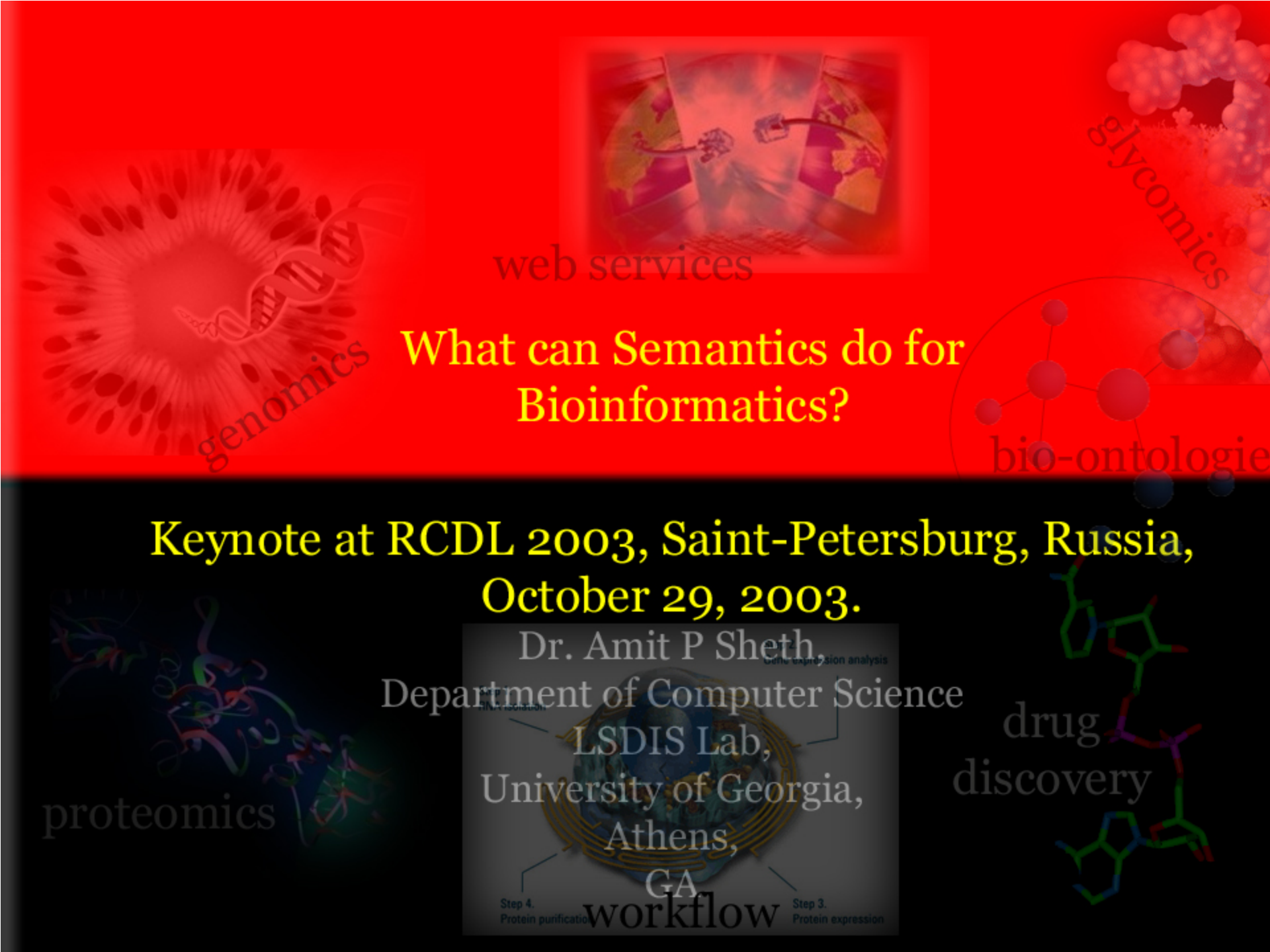
10-29-2003

What Can Semantics do for Bioinformatics?

Amit P. Sheth
Wright State University - Main Campus, amit@sc.edu



What can Semantics do for Bioinformatics?

Keynote at RCDL 2003, Saint-Petersburg, Russia, October 29, 2003.

Dr. Amit P Sheth,
Department of Computer Science
LSDIS Lab,
University of Georgia,
Athens,
GA

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Acknowledgements

UGA Biologists/Biochemists

- Will York, Complex Carbohydrate Research Center
- Jonathan Arnold, Fungal Genomics
- Phillip Bowen, CCQC

Project members of LSDIS lab projects
Bioinformatics for Glycan Expression and METEOR-S (incl. Miller, Kochut, Arpinar)

Special thanks in background research & preparation:
Karthik Gomadam, Christopher Thomas, Kunal Verma

Excellent starting point for complementary material
(a partial list)

- "Building a Bioinformatics Nation," Lincoln Stein's Keynote at O'Reilly's Bioinformatics Technology Conference 2002
- "Bio-Ontologies: Their creation and design" Peter Karp, Robert Stevens and Carole Goble
- "Query Processing with Description Logic Ontologies over Object-Wrapped Databases" Martin Peim, Enrico Franconi, Norman Paton and Carole Goble
- "Ontologies for molecular biology and bioinformatics" Steffen Schulze-Kremer (paper)
- "Can we do better than Google? Using semantics to explore large heterogeneous knowledge sources," Anatole Gershman, SWDB Workshop, 2003.

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Some current BioInformatics Systems

- Tambis
- BioMediator
- Biodas
- BioSem

Data integration, in some cases using an ontology. Single access point for multiple biological information sources; querying multiple sources.

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Outline of this talk...

- A Short History of Science
- Challenges in biology
- What can BioInformatics do for Biology?
- What can Semantics do for BioInformatics?
  - Some examples of Semantics-powered Bioinformatics

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What is difficult, tedious and time consuming now ...

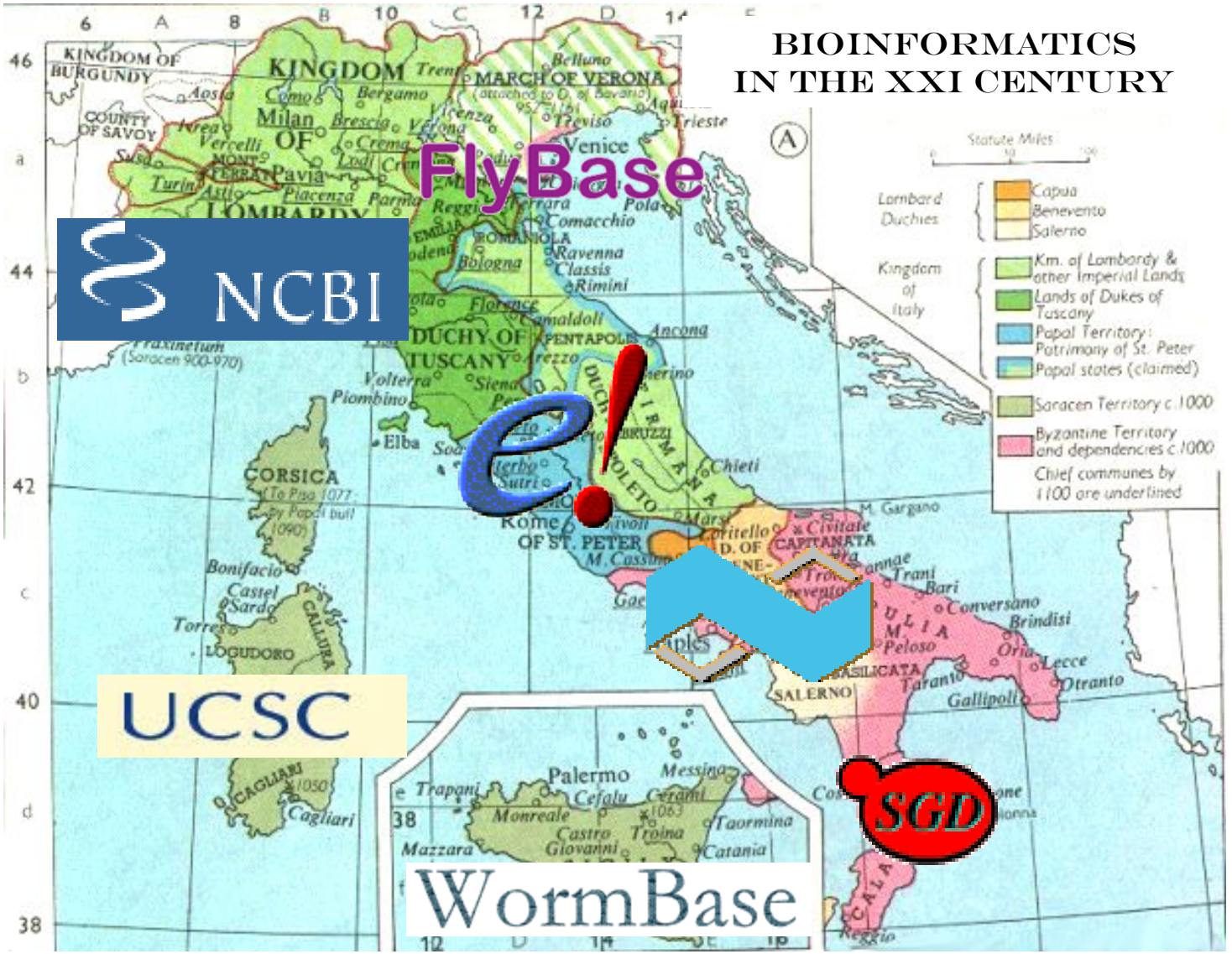
What genes do we all have in common?*

Research to answer this question took scientists two years**

* G. Strobel and J Arnold. Essential Eukaryotic Core, Evolution (to appear, 2003)

**but we now believe with semantic techniques and technology, we can answer similar questions much faster

Why? Bioinformatics, ca. 2002



From http://prometheus.frii.com/~gnat/tmp/stein_keynote.ppt

Science then, then and now

In the beginning, there was thought and observation.

Science then, then and now

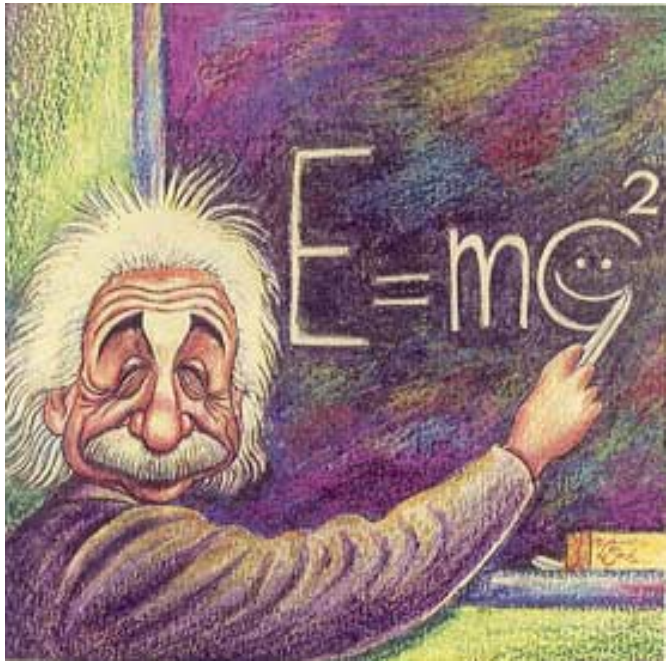
For a long time this didn't change.

- Man thought it would be enough to reason about the existing knowledge to explore everything there is to know.

- Back then, one single person could possess all knowledge in his cultural context.

The achievements are still admirable …

…as we can see



Reasoning and mostly passive observation were the main techniques in scientific research until recently.

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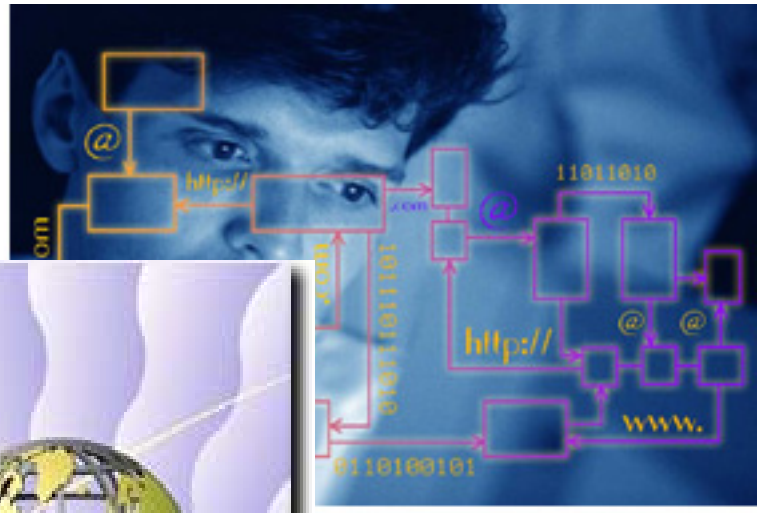
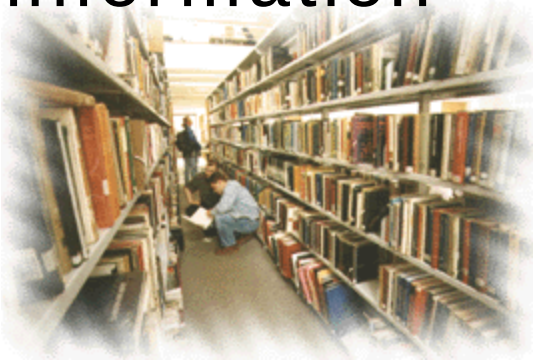
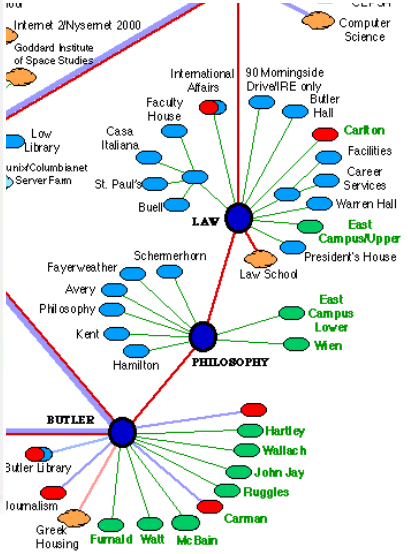
Science then, then and now



A vast amount of information





Science then, then and now

No single person, no group has an overview of what is known.

Known, But not known …→ not known

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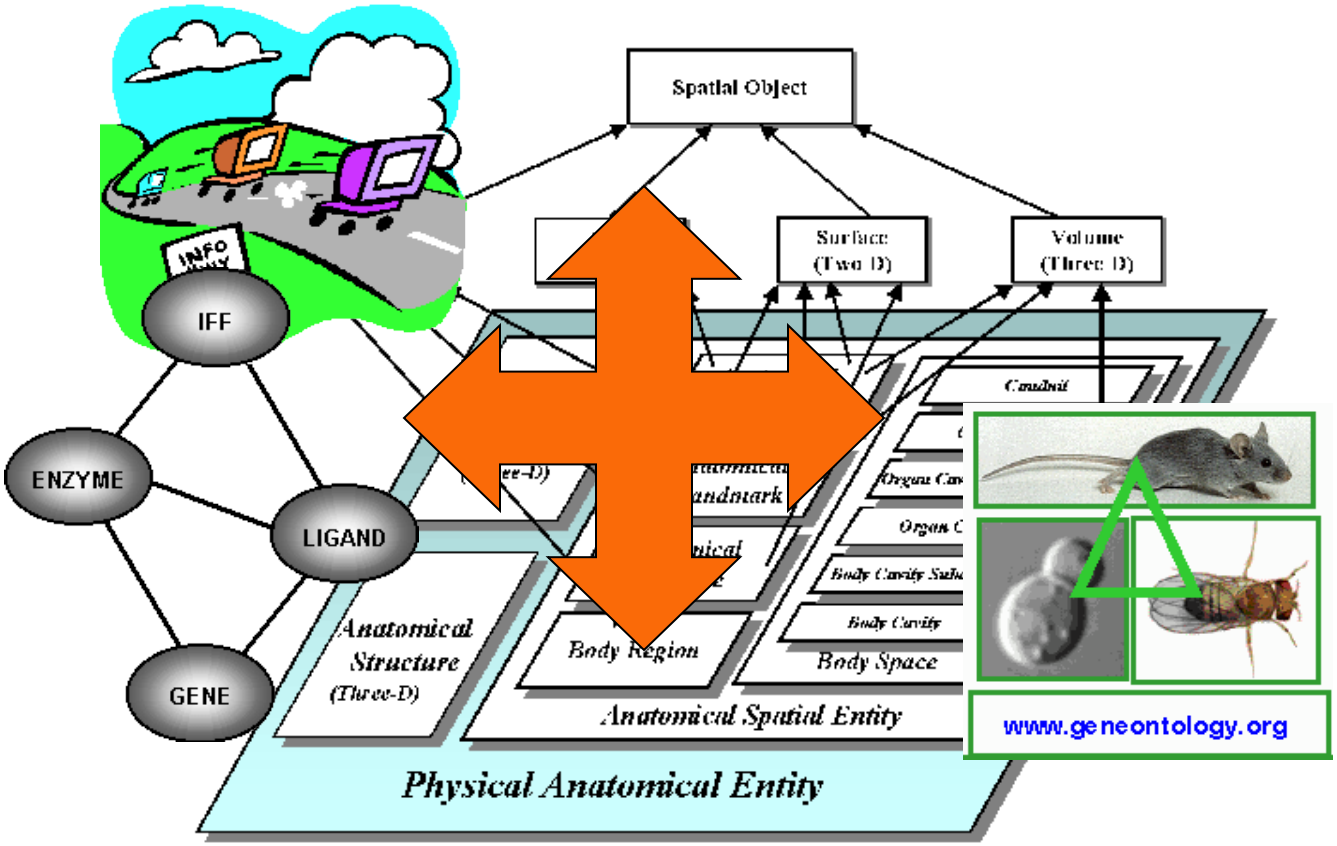
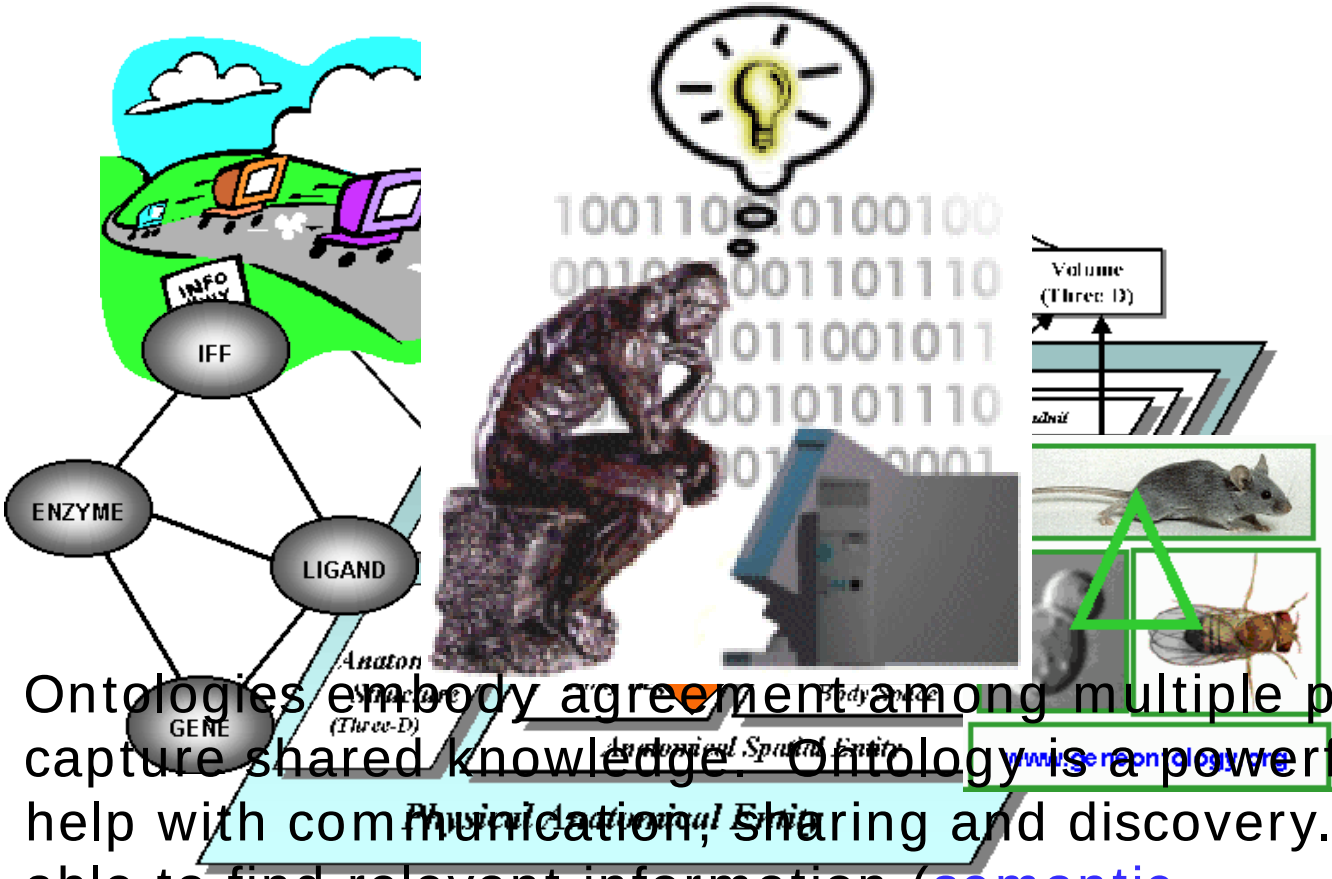
Science then, then and now



Science then, then and now



Ontologies embody agreement among multiple parties and capture shared knowledge. Ontology is a powerful tool to help with communication, sharing and discovery. We are able to find relevant information (semantic search/browsing), connect knowledge and information (semantic normalization/integration), find relationships between pieces of knowledge from different fields (gain insight, discover knowledge)

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bioinformatics

drug discovery

semantic web process

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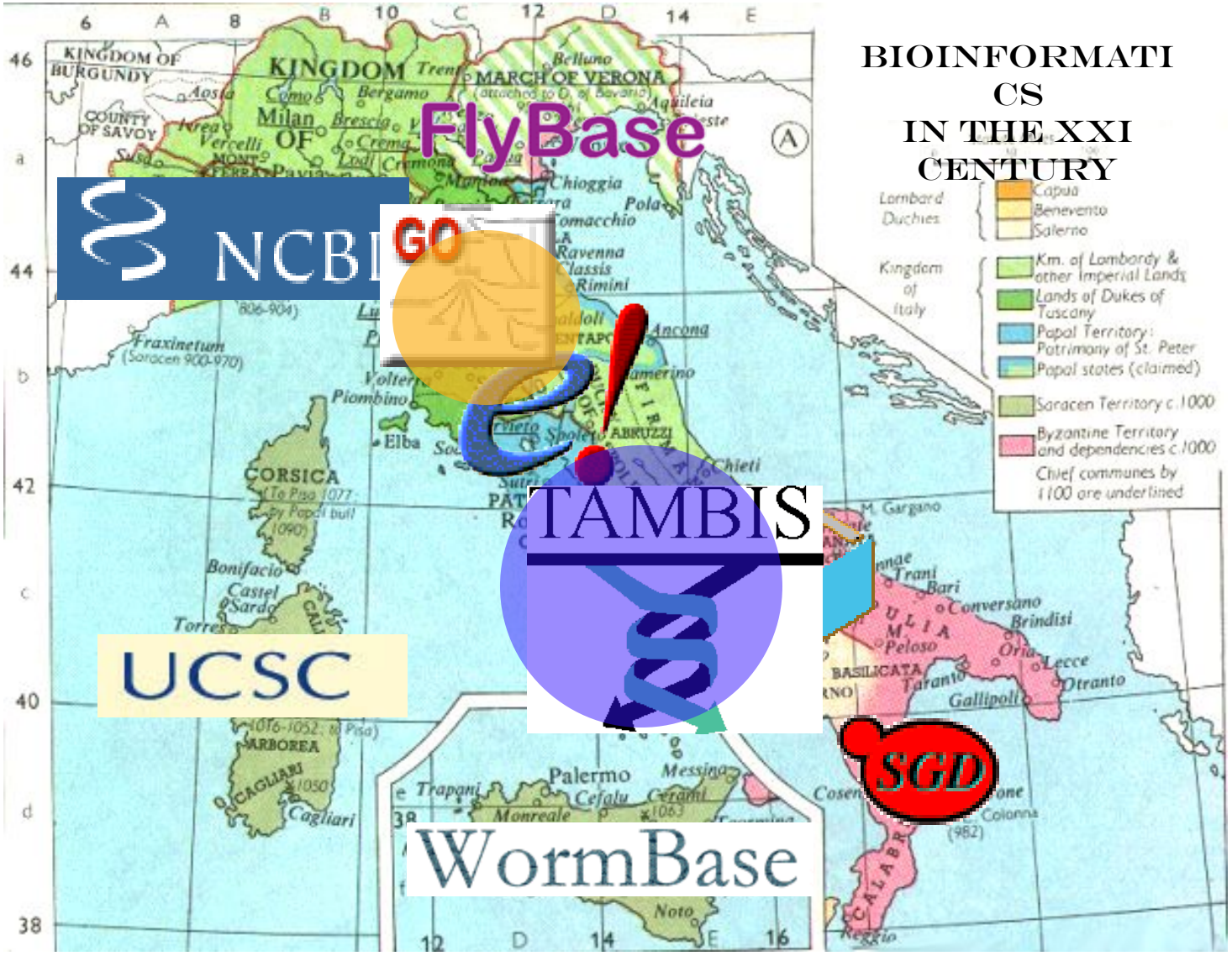
Intervention by Ontologies …



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Outline of the talk…

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- What can BioInformatics do for Biology?
- What can Semantics do for BioInformatics:
  - Some examples of Semantics-powered Bioinformatics

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Challenges in biology

- What makes us ill or unwell?
  - Disease identification, disease inducing agents
- What keeps us healthy and makes us live longer?
  - Drug discovery
- Where do we all come from and what are we made of?
  - Genetics and beyond

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… and their implications

- Understand biological structures of increasing complexity:
  - Genes (*Genomics*): 1980s
  - Proteins (*Proteomics*): 1990s
  - Complex Carbohydrates (*Glycomics*): 2000s
- Understand biological processes and the roles structures play in them (biosynthesis and biological processes)

Outline

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What can BioInformatics do?

- Analyze genetic and molecular sequences
  - Look for patterns, similarities, matches
  - Identify structures
- Store derived information
  - Large databases of genetic information

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Outline

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Paradigm shift over time: Syntax -> Semantics

Increasing sophistication in applying semantics & value add

- **Relevant Information (Semantic Search & Browsing)**
- **Semantic Information Interoperability and Integration**
- **Semantic Correlation / Association, Analysis, Insight and Discovery**

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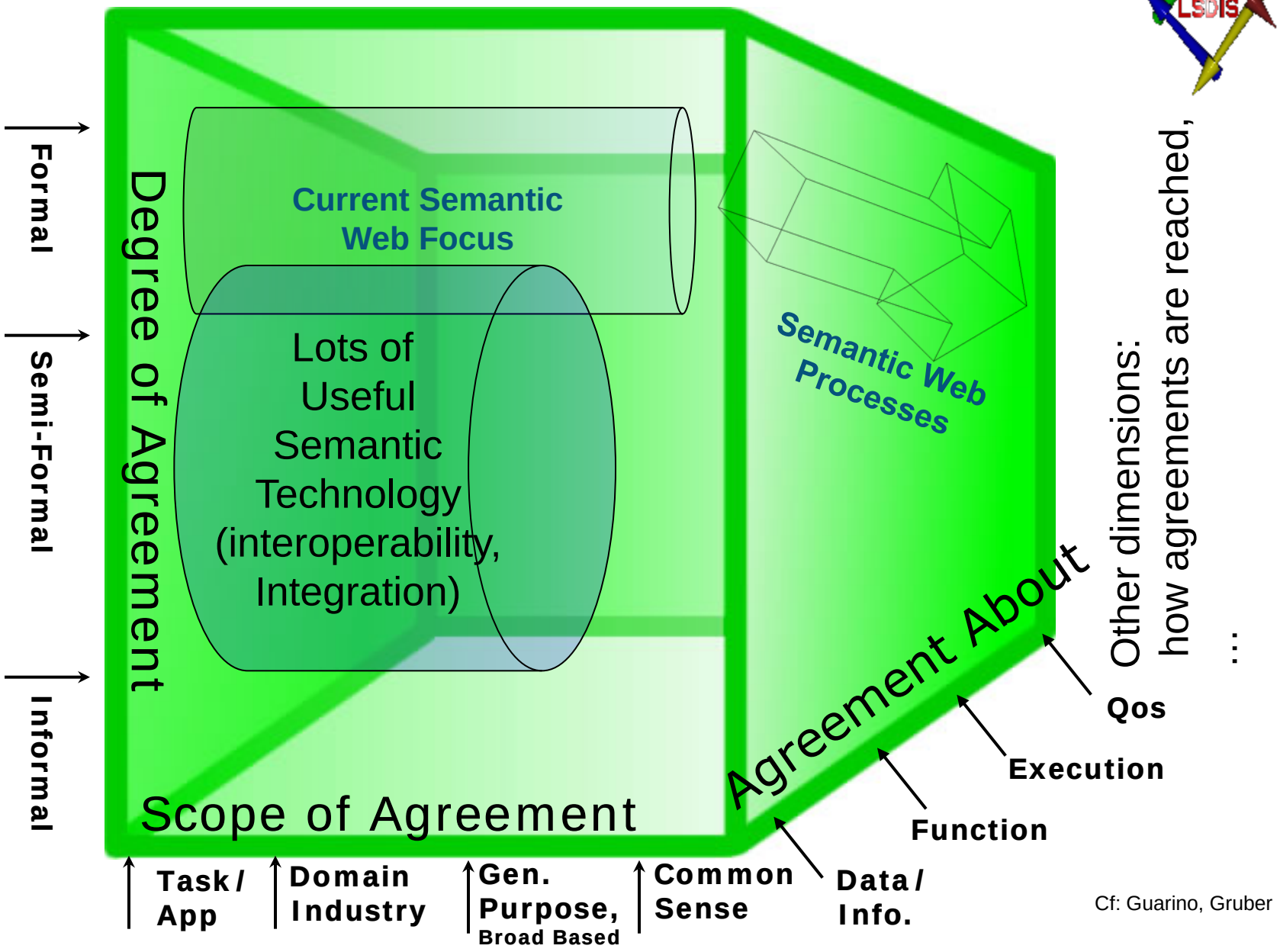
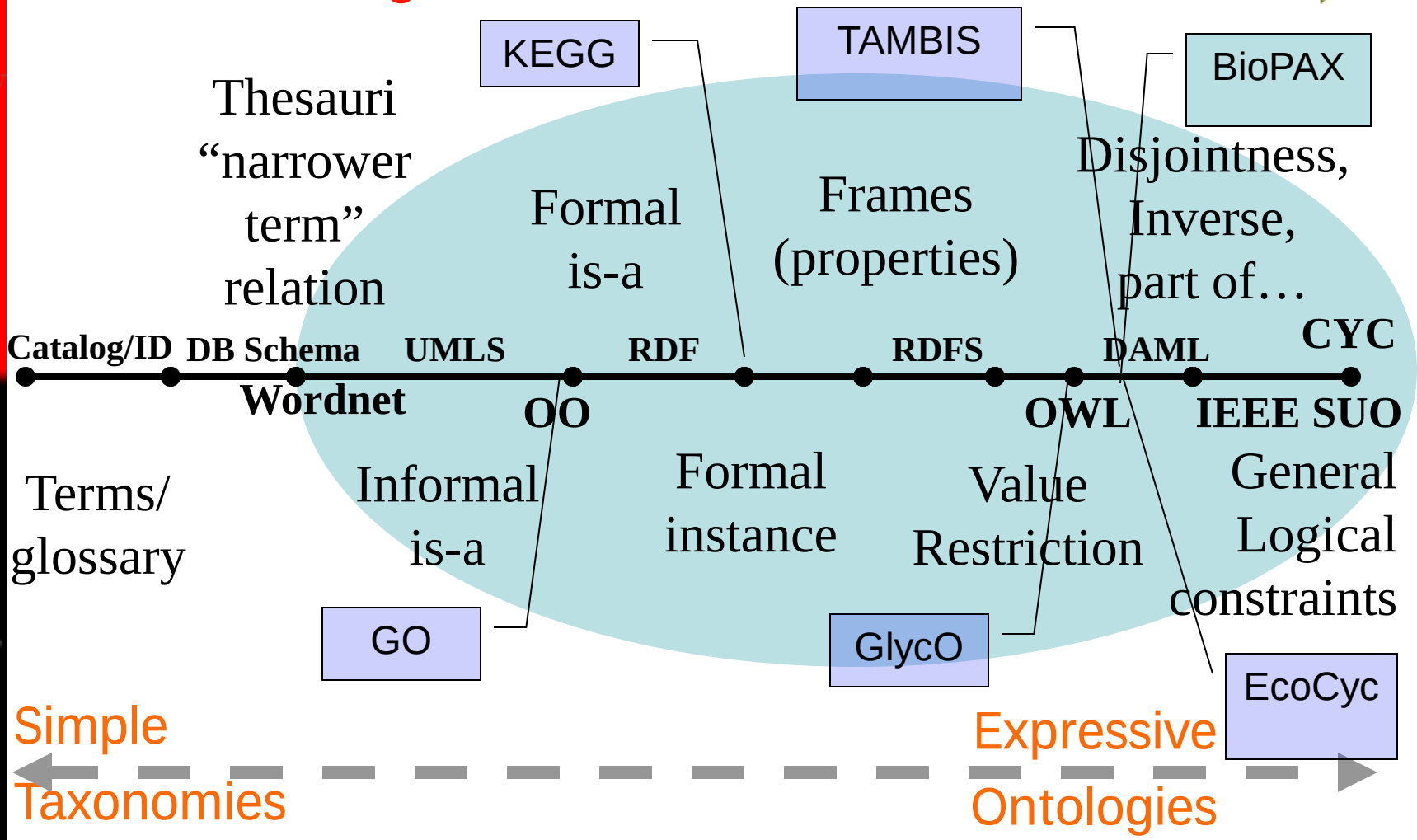
Broad Scope of Semantic (Web) Technology



Cf: Guarino, Gruber

Knowledge Representation and Ontologies



Ontology Dimensions After McGuinness and Finin

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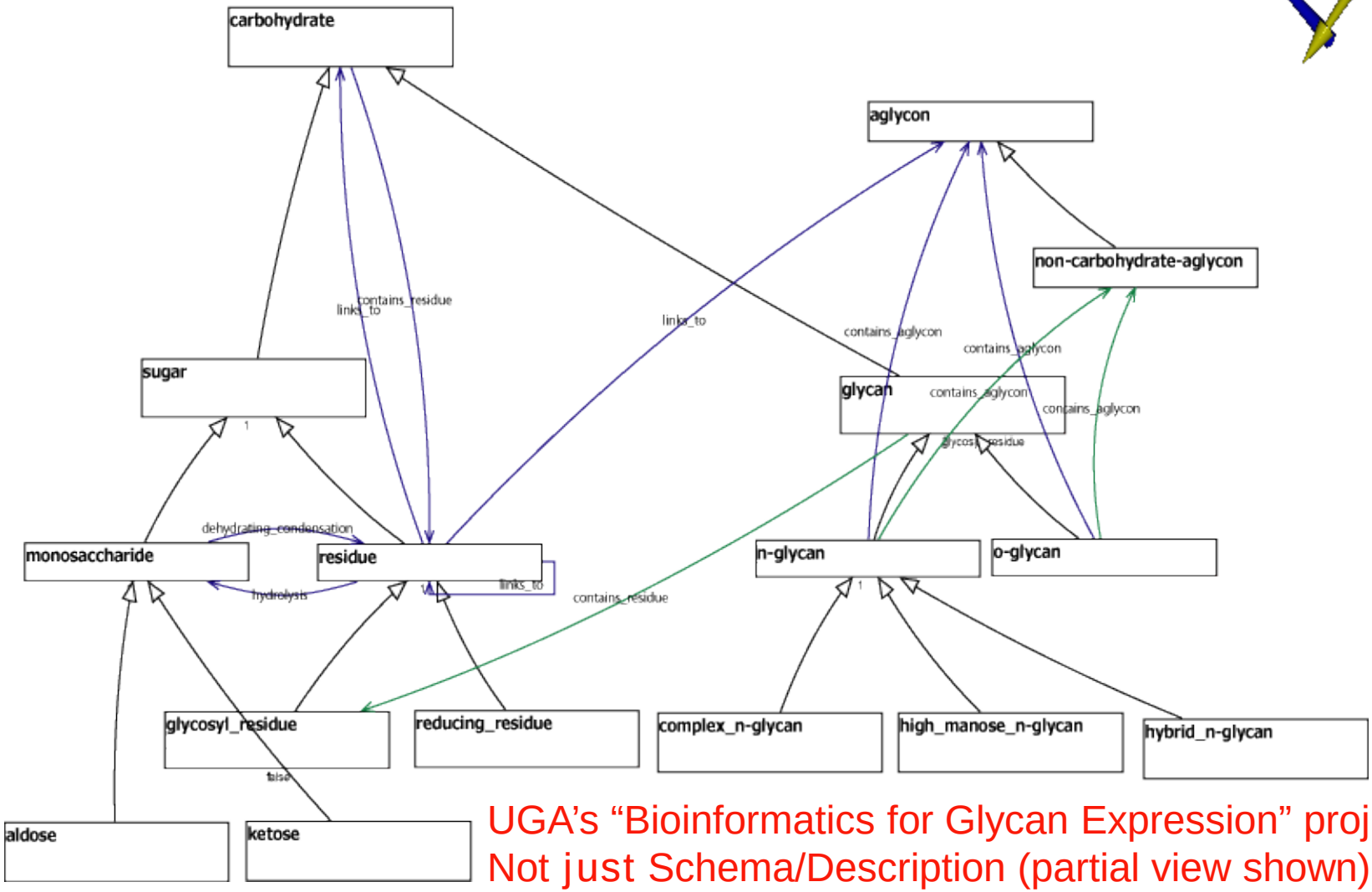
GlycO: Glycan Structure Ontology



UGA's "Bioinformatics for Glycan Expression" proj.
Not just Schema/Description (partial view shown), also description base/ontology population.
In progress, uses **OWL.**

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What can current semantic technology do? (sample)

- Semi-automated (mostly automated) annotation of resources of various, heterogeneous sources (unstructured%, semi-structured, structured data; media content)*
- Creation of large knowledge bases (ontology population) from the trusted sources *
- Unified access to multiple sources*,#
- Inferenceing #
- Relationship/knowledge discovery among the annotated resources and entities; analytics*%
  - Both implicit^ and explicit* relationships

* Commercial: Semagix; %: Near-commercial: IBM/SemTAP;
# Commercial: Network Inference; ^ LSDIS-UGA Research

Industry Efforts

(examples with bioinformatics applications only)

- Accenture's Knowledge Discovery Tool (pre-ontology?, not product)
- Semagix's Semantic Browsing and Querying application for drugs for Rogers MIS and its pharmaceutical customers (product and applications); also semantic analysis application (not discussed here)
- Network Inference's Cerebra server: semantic engineering based bioinformatics system aiding drug discovery (product?)

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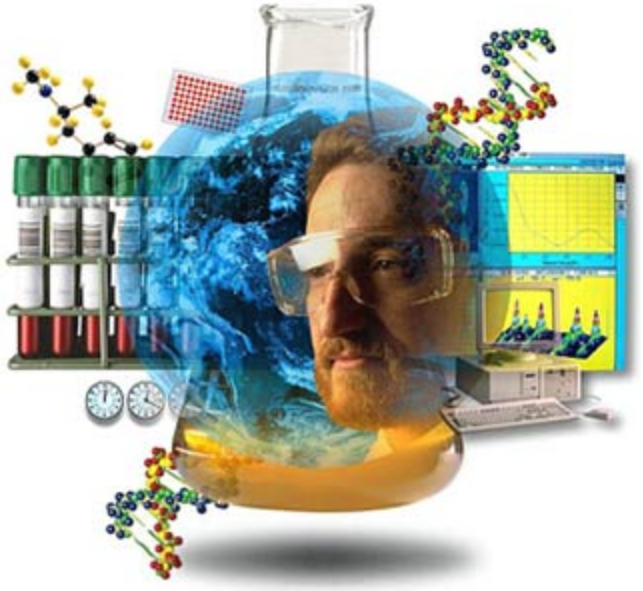
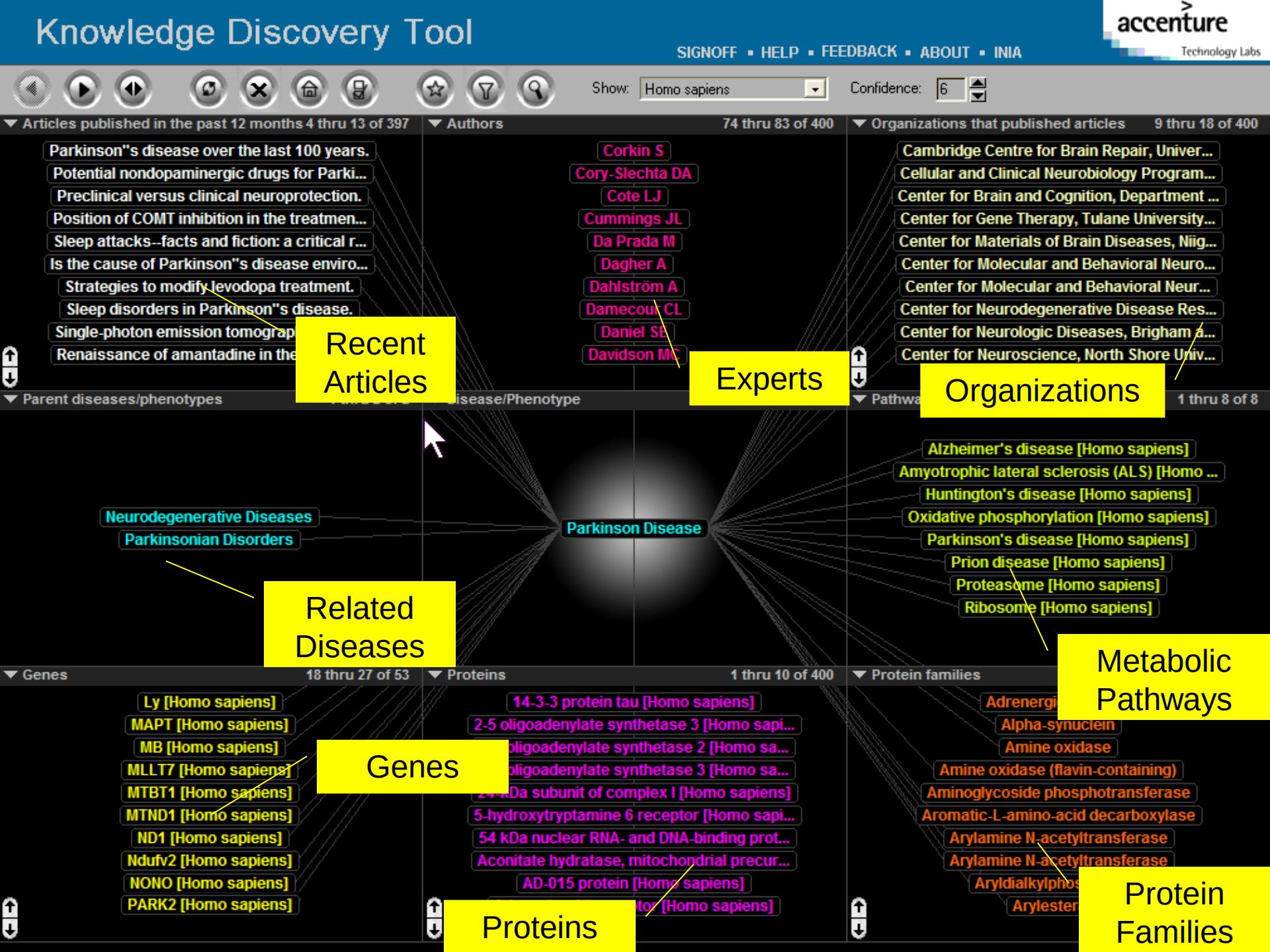
Existing Systems using Semantics for Bioinformatics

FOCUS: SEMANTIC SEARCH AND BROWSING (with nascent work in discovery)




Knowledge Discovery Tool
accenture
Technology Labs
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Show: Homo sapiens
Confidence: 6
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Related Diseases
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Oxidative phosphorylation [Homo sapiens]
Parkinson's disease [Homo sapiens]
Prion disease [Homo sapiens]
Proteasome [Homo sapiens]
Ribosome [Homo sapiens]
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Ly [Homo sapiens]
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NONO [Homo sapiens]
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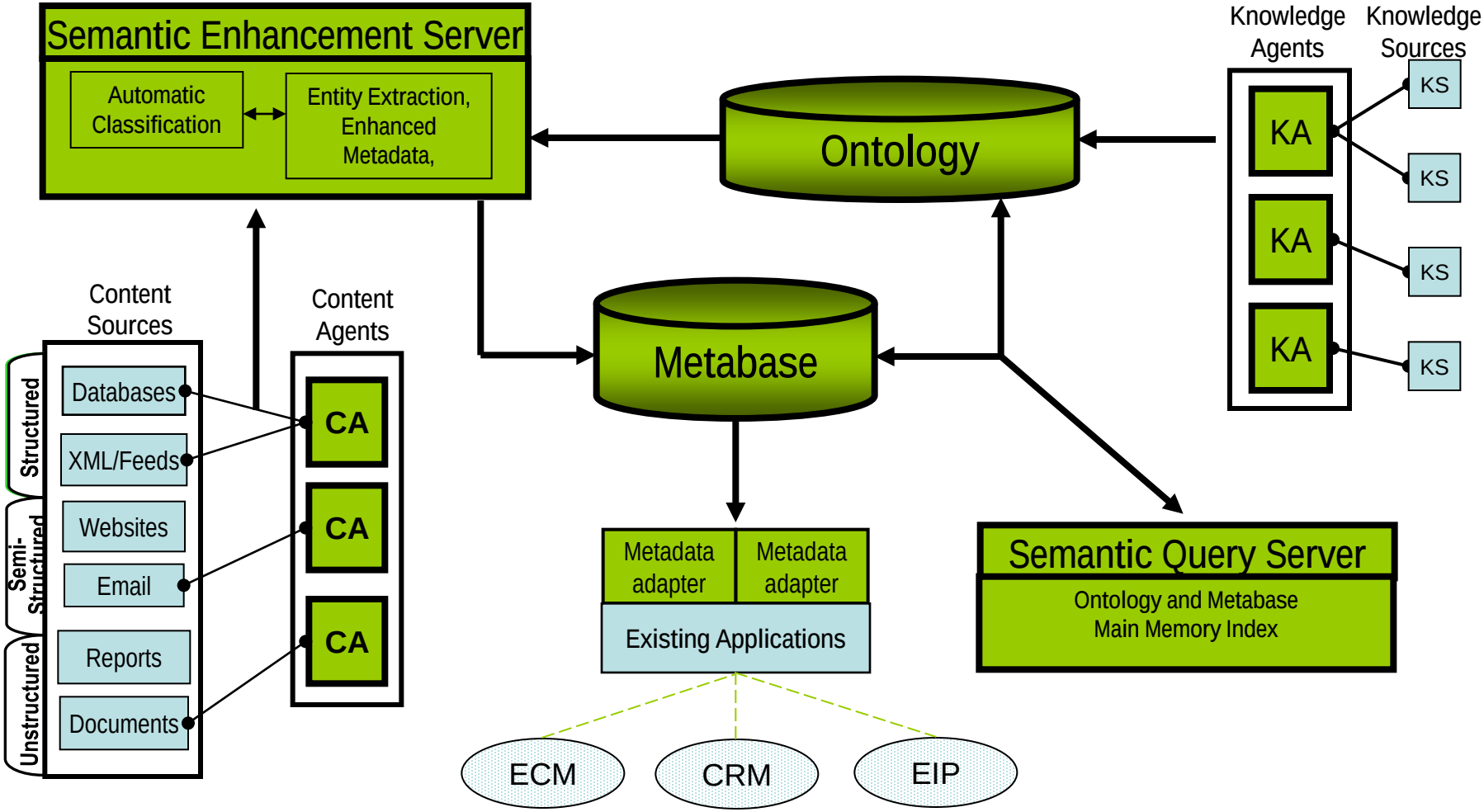
Proteins
Protein families
Adrenergi
Alpha-synuclein
Amine oxidase
Amine oxidase (flavin-containing)
Aminoglycoside phosphotransferase
Aromatic-L-amino-acid decarboxylase
Arylamine N-acetyltransferase
Arylamine N-acetyltransferase
Aryldialkylphos
Arylester
Protein Families

Semagix Freedom Architecture

(a platform for building ontology-driven information system)

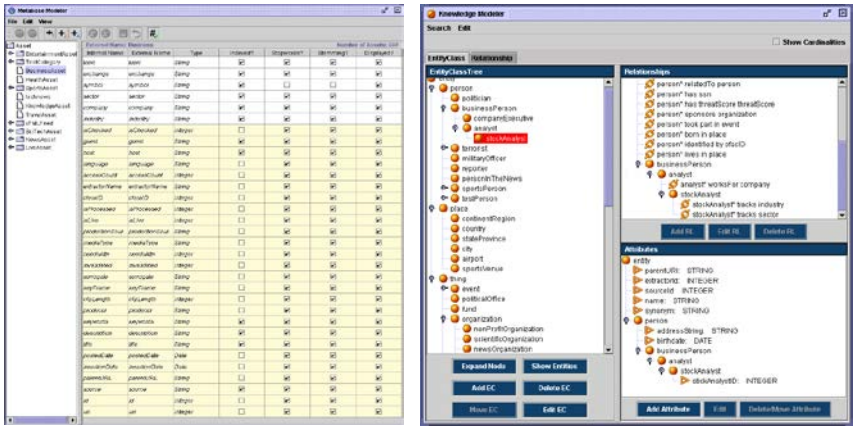


Semagix

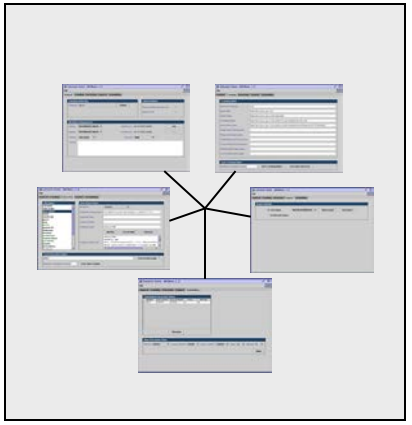
Ontologies Semagix has designed:

- Few classes to many tens of classes and relationships (types); very small number of designers/knowledge experts; descriptional component (schema) designed with GUI
- Hundreds of thousands to over 10 million entities and relationships (instances/assertions/description base)
- Few to tens of knowledge sources; populated mostly automatically by knowledge extractors
- Primary scientific challenges faced: entity ambiguity resolution and data cleanup
- Total effort: few person weeks
- Key requirement: trusted knowledge sources

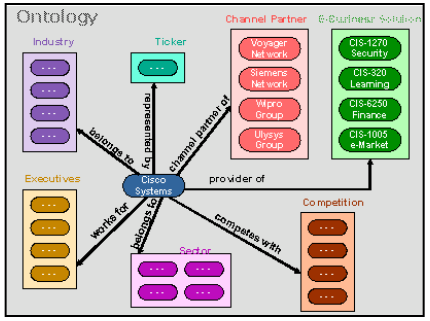
Ontology Creation and Maintenance Steps



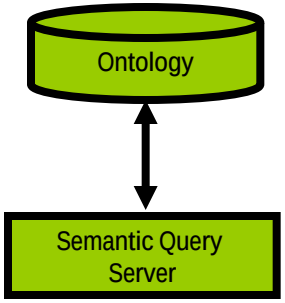
1. Ontology Model Creation (Description)



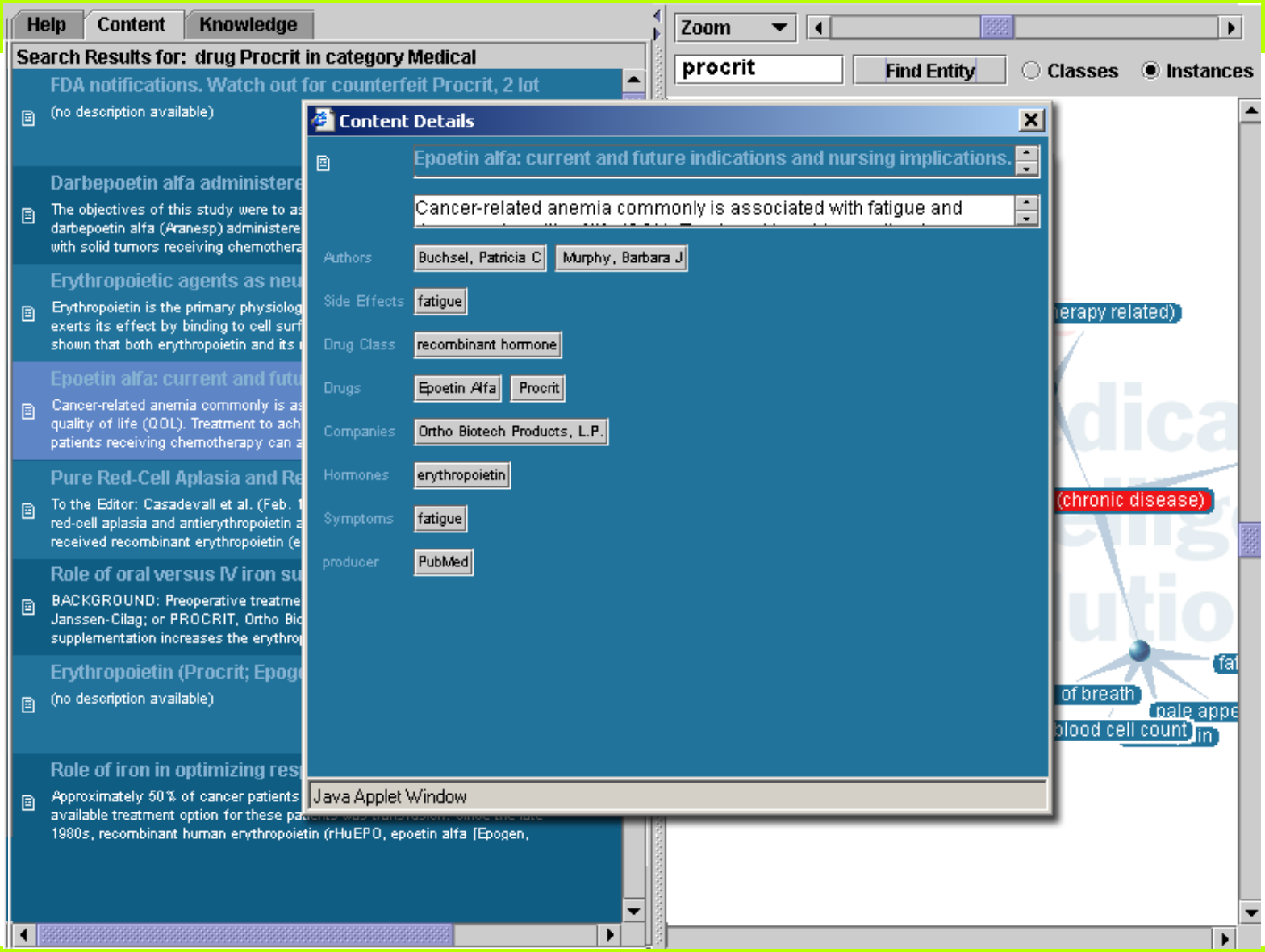
2. Knowledge Agent Creation



3. Automatic aggregation of Knowledge



4. Querying the Ontology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Role of iron in optimizing res
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available treatment option for these pa
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Epoetin alfa: current and future indications and nursing implications.
Cancer-related anemia commonly is associated with fatigue and
Authors
Buchsel, Patricia C
Murphy, Barbara J
Side Effects
fatigue
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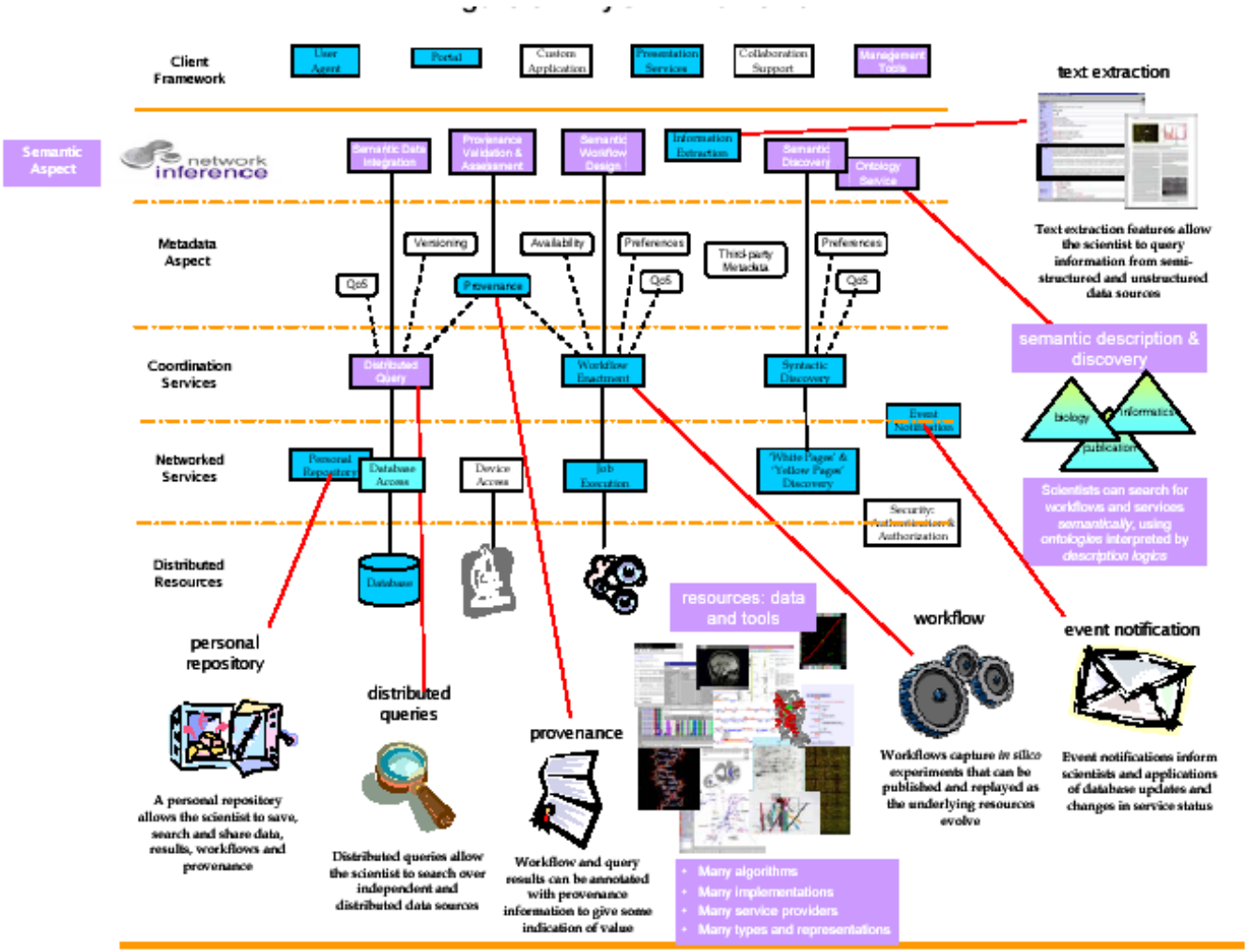
Cerebra's myGrid Framework



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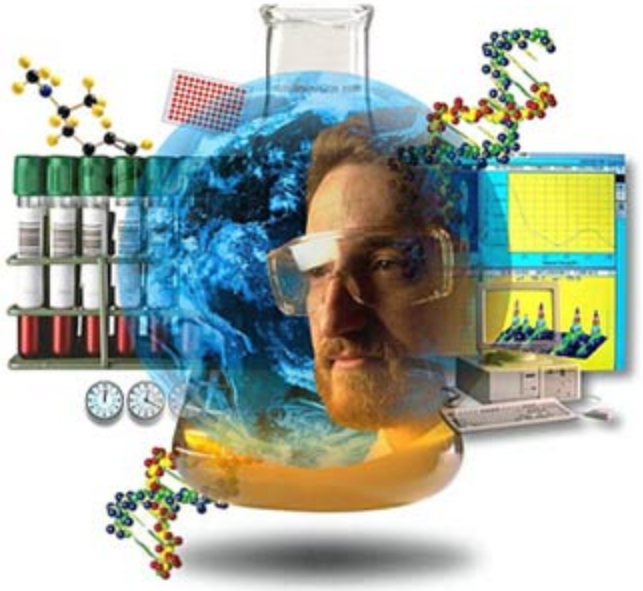
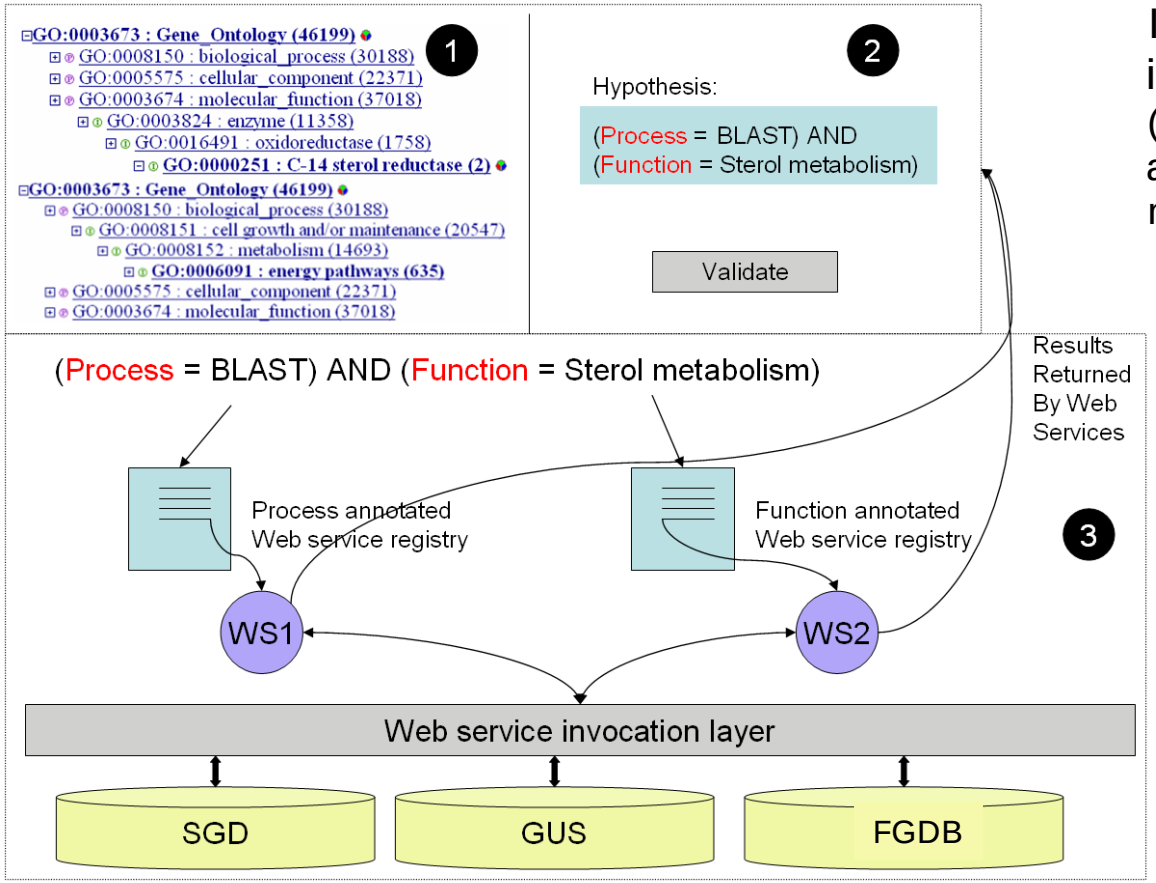
Applying Semantics to BioInformatics : Example 1

Semantic Browsing, Querying and Integration



Semantic Querying, Browsing, Integration to find potential antifungal drug targets



Is this or similar gene in other organism? (most Antifungals are associated with Sterol mechanism)

Services: BLAST, Co-expression analysis, Phylogeny; If annotated, directly access DB, else use BLAST to normalize

Databases for different organisms

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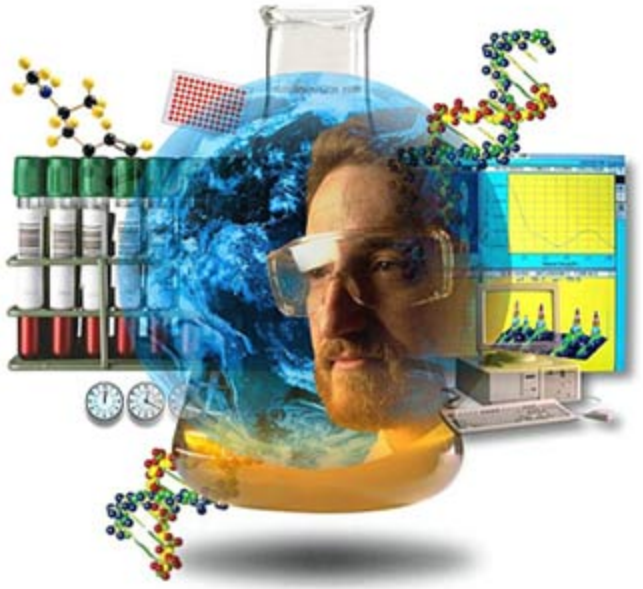
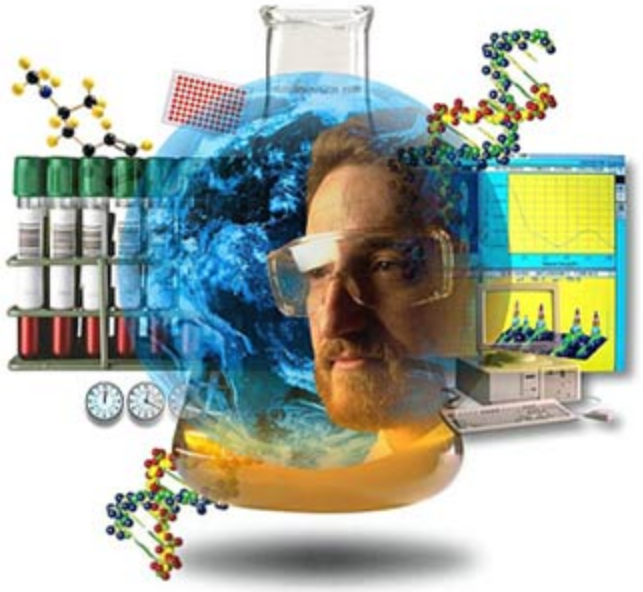
Applying Semantics to BioInformatics : Example 2

Analytics in Drug Discovery

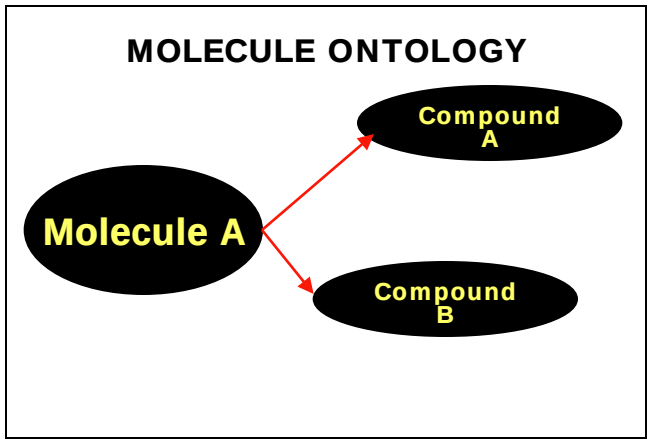


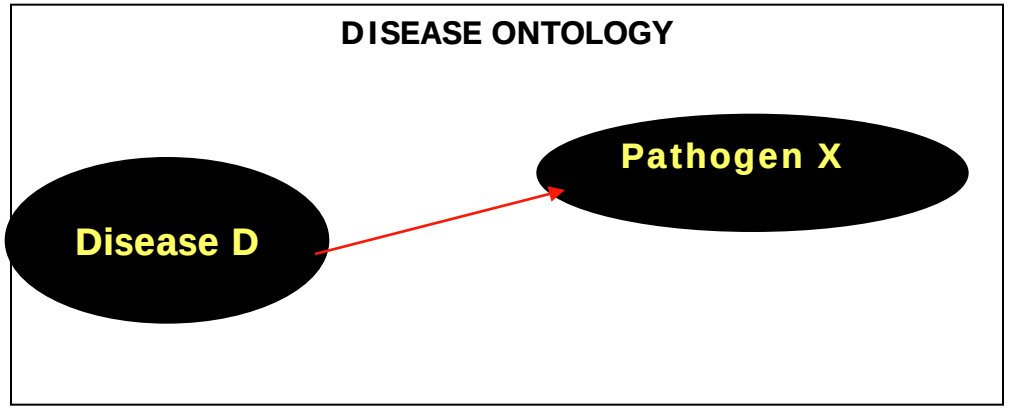
Analytics, Using Explicit and Implicit Relationships in Drug Discovery

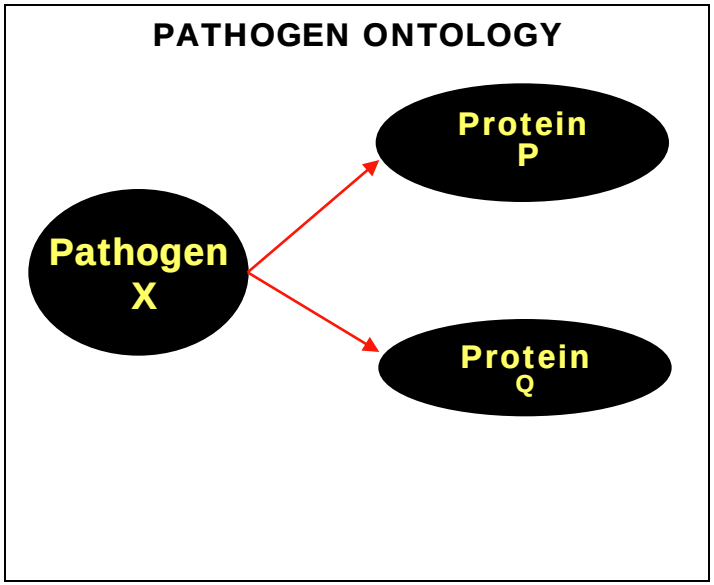
- Some molecules contain functional groups that inhibit them from acting as drugs
- Elimination of these groups can make the molecule, a DRUG.



Step 1: Capture domains using ontologies







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Step 2: Traverse explicit relationships

STEP 3 (Molecule Ontology):

1. Look up the molecule ontology
2. Identify the composition of the possible drug.

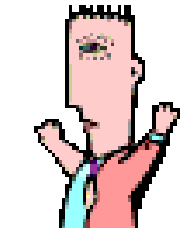
STEP 1 (Disease Ontology):

1. Look up the disease ontology
2. Identify the disease causing pathogen.

STEP 2 (Pathogen Ontology):

1. Look up the pathogen ontology
2. Identify the molecular composition of the pathogen.

Step 3: Discovering Implicit relationships…



Extract the relationships amongst the compounds of the potential drug and the pathogen.

Compound A inhibits protein P

Compound B inhibits protein Q

Compound A and B together inhibit protein P by killing protein Q

Inferences Based on Relationships

- Compound B doesn't contribute to the curing aspect of the drug, but rather generates a toxin.
- Eliminate compound B and molecule A can be a potential drug.
- However if the host has protein P, then we cannot use protein to bind the drug.
- So look for another drug that can bind at protein Q without producing a toxin
- Eliminate and Discover!!!!

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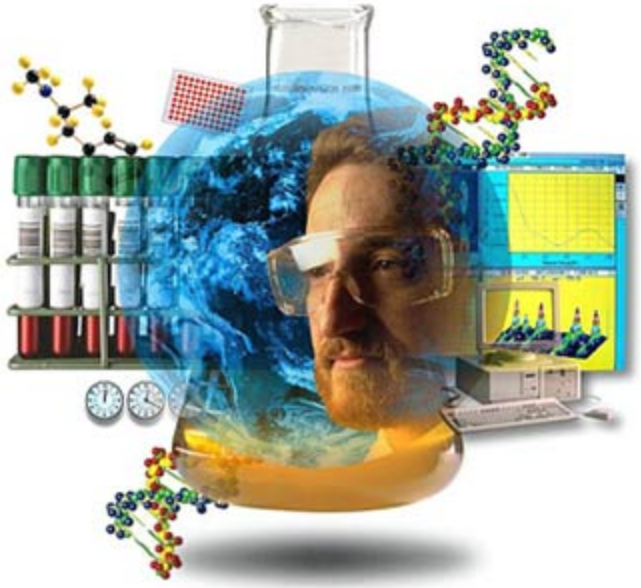
Applying Semantics to BioInformatics : Example 3

Using Ontologies in cancer research



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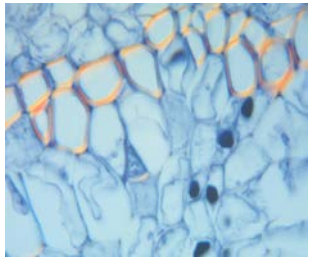
Disparate Data from Different Experiments

Experiment 1



Metastatic cancer cells

Increased GNT-V Activity

Experiment 2

Cancer marker glycan sequence elevated in glycoprotein beta 1 integrin

Knowledge Stored in Ontologies

- GO Ontology
  - GNT V is an enzyme involved in production of N-glycans
- Glycan Structure Ontology (GlycO)
  - Sequences and structures of Glycans
- Extended Structure Ontology
  - How the structures are made
    - E.g GNT V produces certain class of N-Glycans

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Finding New Information

- Combine data from experiments and knowledge stored in ontologies
- Known assertion from Experiments
  - Beta Integrin is involved in cancer
- New assertion to be tested
  - Are any other glycoproteins involved in cancer ?

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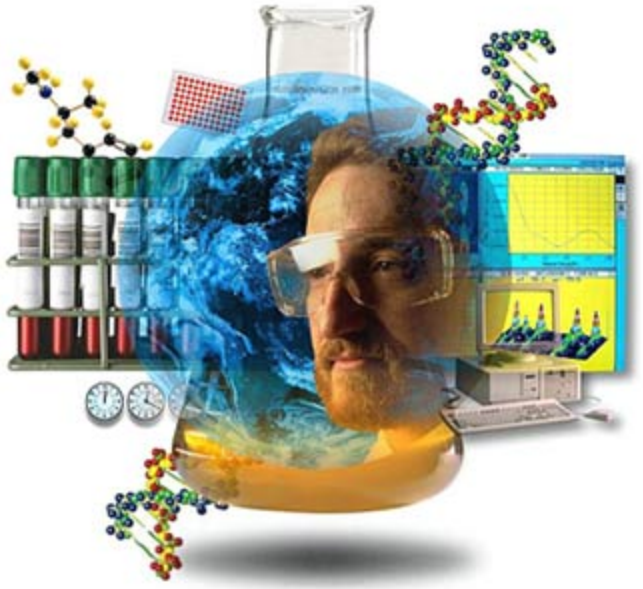
Applying Semantics to BioInformatics : Example 4

Applying Semantics to BioInformatics Processes



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Creating BioSemantic Processes

- **Question: *What essential genes do we all have in common?***
- Research process for this using current techniques takes long time (2 years)
  G. Strobel and J Arnold. Essential Eukaryotic Core, Evolution (to appear, 2003)
- Let us demonstrate use of Functional, Data, QoS and Execution Semantics to automate the process and reduce time

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Creating BioSemantic Processes

Process for the question:

1. Input GO Id of relevant gene
2. Retrieve similar sequences
3. Perform multiple sequence alignment
4. Construct phylogenetic tree

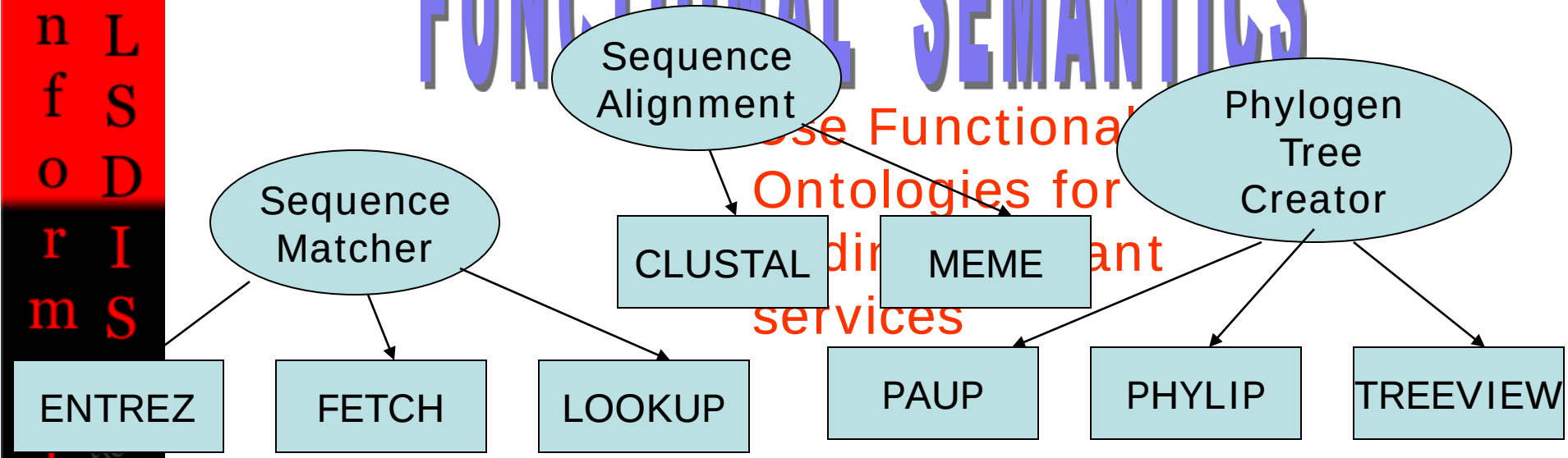
BioSemantic Process Definition

- Create semantically annotated Web Services (wrapping tools) and process using METEOR-S
- Semantic templates at each node allow choosing multiple tools automatically
- Run multiple instances of process using different tools, combine results

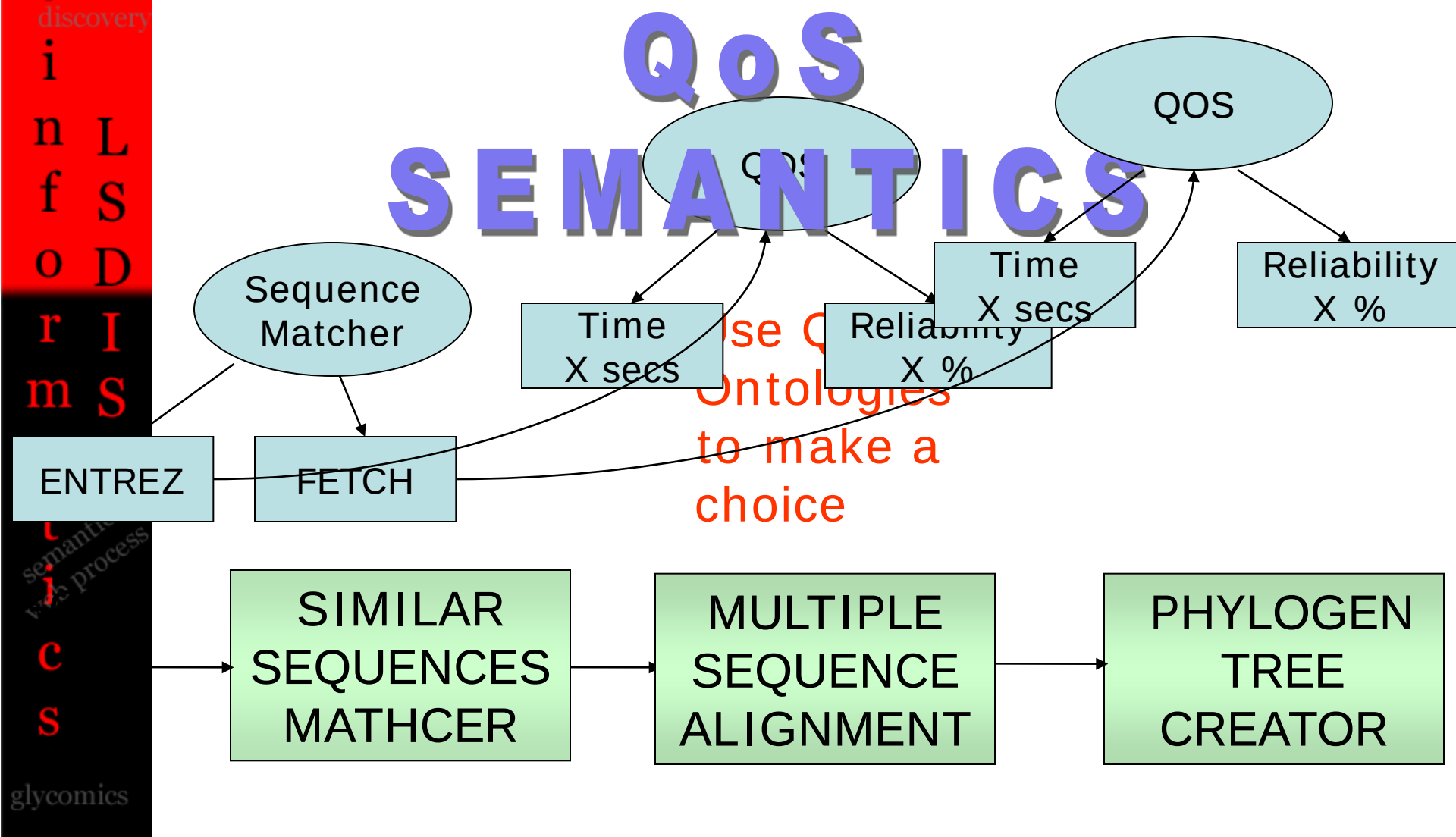
Semantic Bioinformatics Processes

FUNCTIONAL SEMANTICS

Use Functional Ontologies for discovery relevant services



Semantic Bioinformatics Processes



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Semantic Bioinformatics Processes

DATA SEMANTICS

MAY REQUIRE DATA CONVERSION

MAY REQUIRE DATA CONVERSION

Use Concept Ontologies for Interoperability

SIMILAR SEQUENCES MATHCER

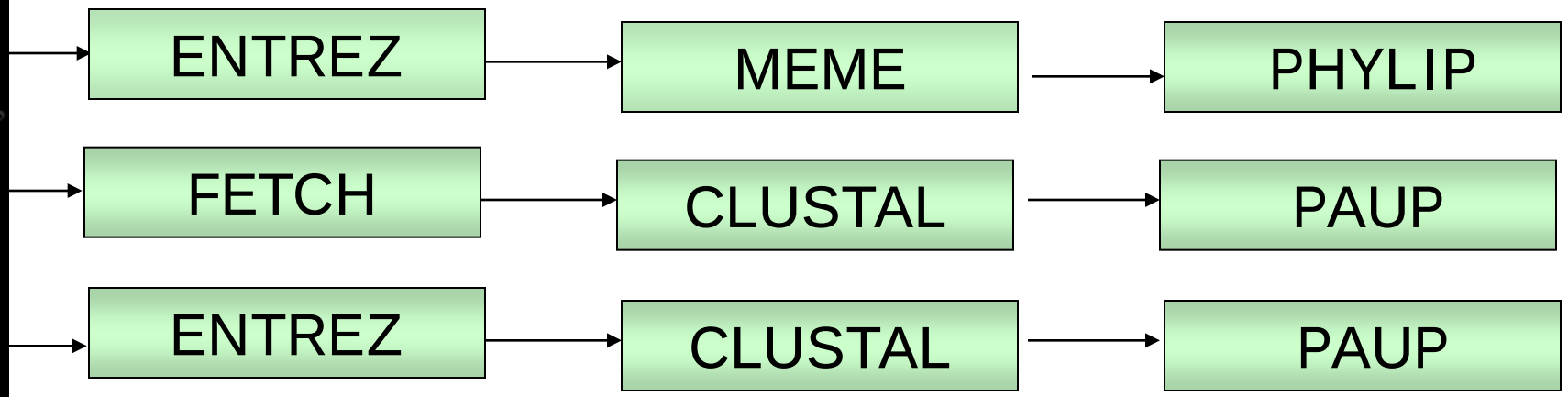
MULTIPLE SEQUENCE ALIGNMENT

PHYLOGEN TREE CREATOR

Semantic Bioinformatics Processes

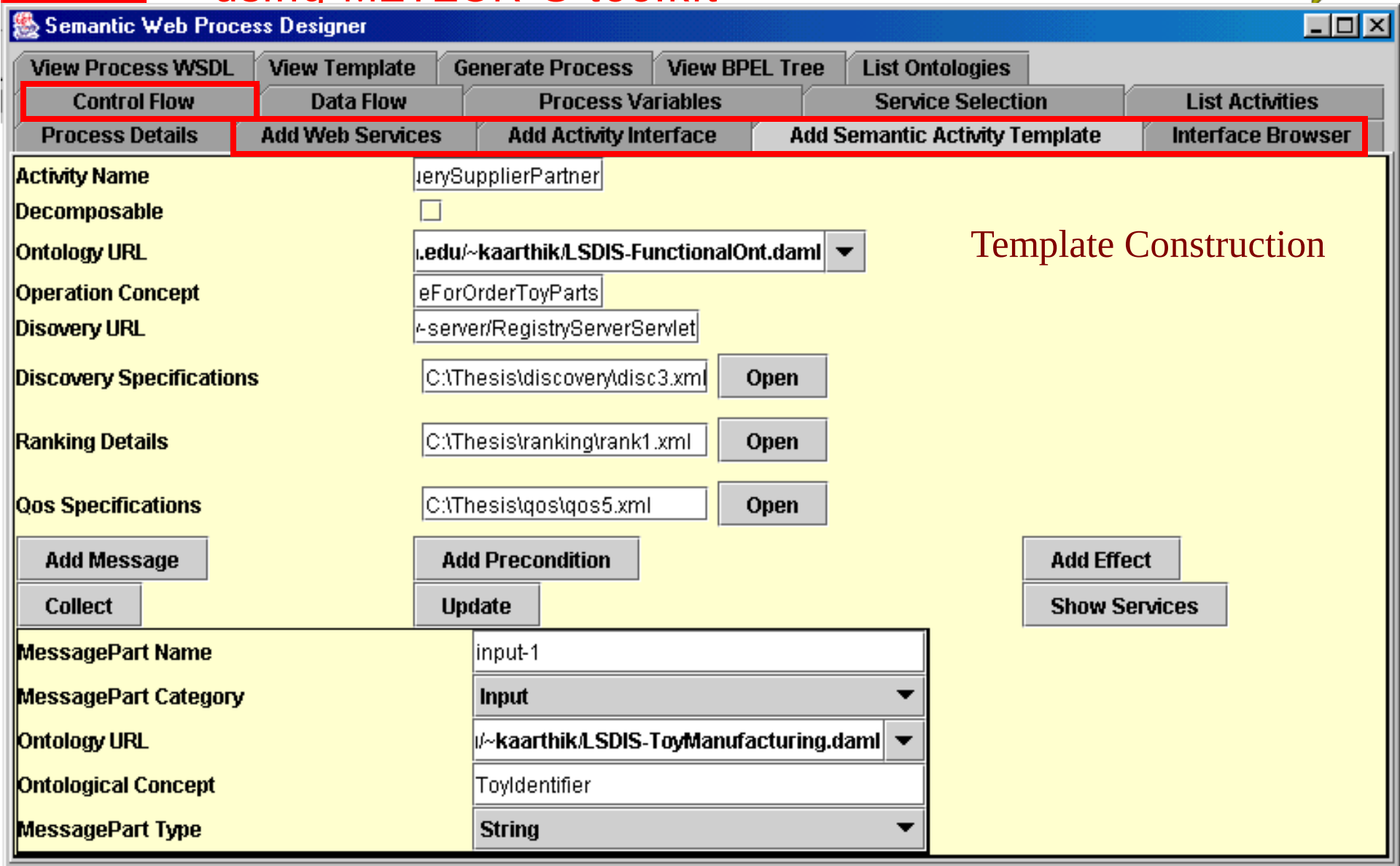
EXECUTION SEMANTICS

Use Execution Semantics for execution monitoring of different instances



Semantic Web Process Mgmt

using METEOR-S toolkit



Template Construction

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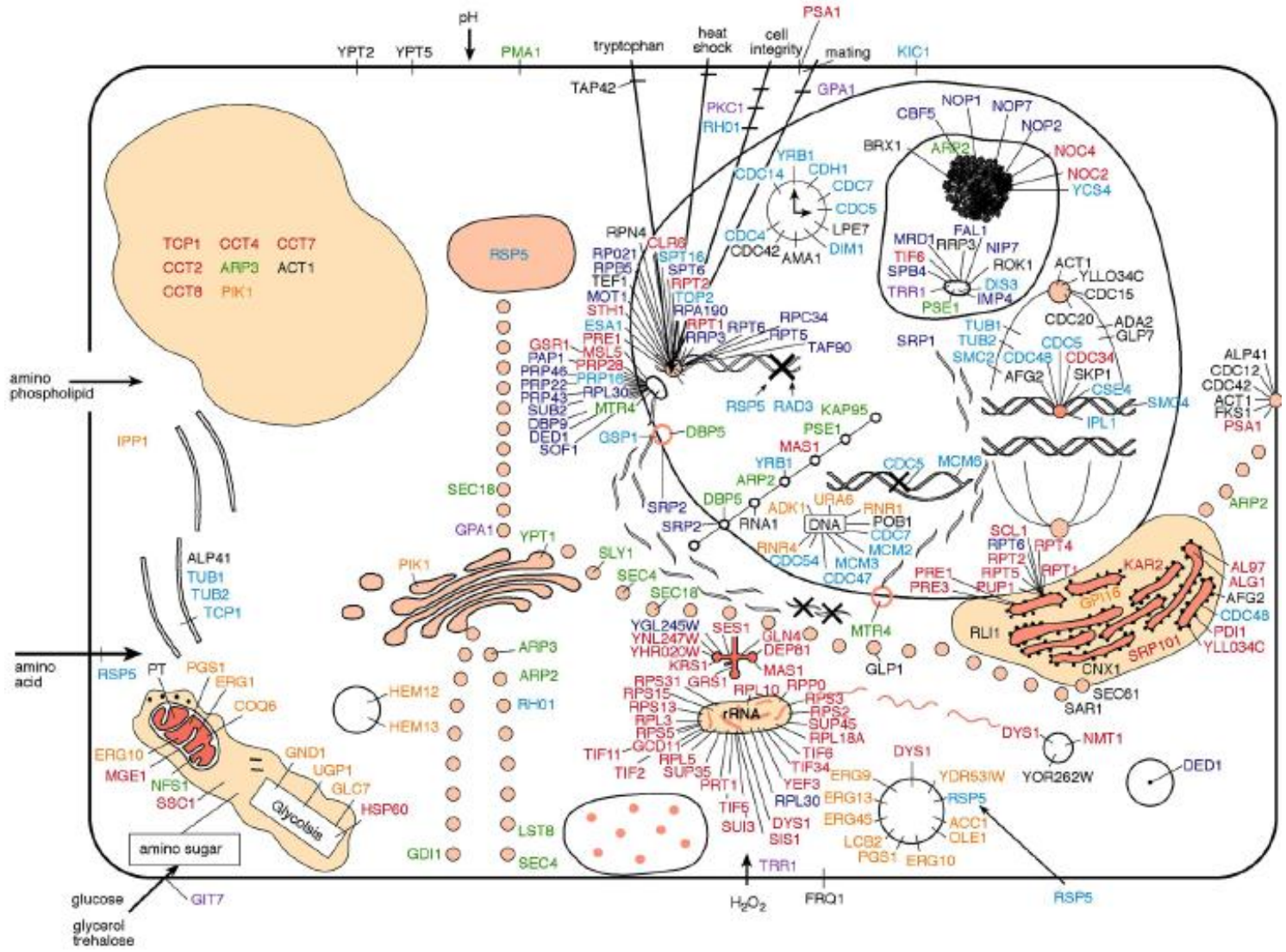
LSDIS

Common genes



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Conclusion

- Biology research at unique standpoint in history
- Earlier
  - Biology divided into many sub-fields
  - Significant progress in those domains
- Present
  - Searching for the bigger picture
  - Need to combine knowledge from sub-fields
    - Disparate sources, terminologies
- Semantics is the vehicle to get to the answers

Conclusion

- Need to capture the bioinformatics domains using ontologies
  - Not just schema, instances are required
- Presented the use of semantics in
  - Search, Integration
  - Analytics, Knowledge discovery
  - Process Automation
- Collaboration between scientists and computer scientists with semantic techniques and tools make hard things easier

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Sources

1. Picture on each sub-section title : http://www.3rdMill.com
2. Pictures on the title collage were taken from
   - http://web.mit.edu/beh.480j/www/covermed.gif - Glycomics
   - http://bcf.bcm.tmc.edu/proteomics_3.jpg - Proteomics
   - http://www.microsoft.com/spain/msdn/eventos/presentaciones/images/ - Webservices
   - http://panda.cs.inf.shizuoka.ac.jp/~cs8060/images/ontology.png - ontology
   - http://www.chem.agilent.com/cag/other/workflow-330.gif - RNA analysis workflow
   - http://www.exploratorium.edu/ti/human_body/dna.html - Genomics
   - Molecular Modelling – Principles and Applications by Andrew R Leach - Drug Discovery

Bioinformatics and Semantic Web at LSDIS Lab, UGA:
http://lsdis.cs.uga.edu/proj/glycomics/

Also, Semantic Web Processes: http://swp.semanticweb.org